REMARKS

Claims 8 and 33-37 have been canceled without prejudice. Claim 1 has been amended to more particularly point out the claimed subject matter. Support for the claim amendments can be found throughout the specification (e.g., page 5, lines 5-17; pages 12, lines 7-9; and Table 1 on pages 79-81). No new matter has been introduced. Applicants submit that the amendments are made merely to expedite allowance of claims directed to most commercially relevant embodiments of the present invention. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants note that the Examiner has withdrawn the previous rejections under 35 U.S.C. § 112, first paragraph (written description), under 35 U.S.C. § 112, second paragraph, and under 35 U.S.C. § 102(e) (citing Katz et al., and Warrington et al., respectively).

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Election/Restriction

The Examiner has acknowledged Applicants' election, with traverse, of Group I (claims 1-11) and the species election of mRNA in the Response filed on October 2, 2006.

Priority

The Examiner maintains that the claims presently have a priority date of January 29, 2002. Applicants reserve the right to traverse the Examiner's assertion until allowable subject matter is found; at which point, Applicants will provide supportive priority documents if deemed necessary.

Sequence Compliance

The Examiner has acknowledged that the application is presently in compliance with the sequence rules.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-6, 8-10, and 33-37 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner asserts that this is a new matter rejection. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action asserts that "the specification as originally filed does not provide support for the specific sequences of SEQ ID NOs: 1-43 (see present claims 1, 8, 33, and 36), an open ended range of 'at least 40 genes' (see present claim 1), a random subset of 40 genes from the group consisting of SEQ ID NOs: 1-43 (see present claim 1) which is diagnostic, a subset of SEQ ID NOs: 1-43 (see present claim 33), a random subset of 5 genes from the group consisting of SEQ ID NOs: 3, 5, 10, 15, 16, 21, 22, 27, 28, 31, 32, 35, 37, and 40 (see present claim 33) which is diagnostic, a subset of SEQ ID NOs: 3, 5, 10, 15, 16, 21, 22, 27, 28, 31, 32, 35, 37, and 40 which is diagnostic (see present claim 36), and 'comparing the test expression profile with at least one signature expression profile [from] a patient known to have an oral cancer' (see present claims 1 and 33). Applicants have not provided evidence that the specific sequences of SEQ ID NOs: 1-43 were associated with the accession numbers, gene names, chromosome locations, or functions in originally disclosed Table 1 at the time of filing." Office Action, the paragraph bridging pages 7 and 8.

Solely to expedite prosecution, Applicants have canceled claims 8 and 33-37 without prejudice. Applicants have amended independent claim 1 to define the 45 genes by including their accession numbers, rather than SEQ ID NOs. Claim 1 as amended recites a method for diagnosing an oral cancer in a patient, comprising: a) obtaining a biological sample from a patient; b) determining the expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile, wherein the plurality of genes have GenBank Accession Nos. X76029, U34252, U47011, M34309, U58970, D42047, M69177, X02419, X78932, Z78289, U46689, Y09616, M57731, M14200, U07969, M74558, S45630, Z29083, U56814, X15183, U59919, M19961, HG3549-HT3751, U18934, X87241, J04469,

M11147, U19345, L14848, D13643, U06643, X98085, M28825, M61855, U24577, HG2992-HT5186, Z78285, D79994, L19593, M30818, U67963, U11877, X07695, D43968, and X12451; and c) comparing the test expression profile with at least one signature expression profile from a patient known to have an oral cancer, wherein said signature expression profile consists of said plurality of genes and is indicative of an oral cancer, wherein if the test expression profile substantially matches said signature expression profile, the patient has the oral cancer.

Applicants submit that the specification provides sufficient descriptions of the method as recited in amended claim 1. For example, the specification on page 5, lines 5-17, teaches that "Applicants have discovered a set of genes that are differentially expressed in oral cancer cells versus normal cells. Applicants have shown that the expression profile of this set of genes is indicative of oral cancer, and as such, constitutes a signature expression profile of oral cancer. Thus, measuring expression levels of these genes in a sample cell population allows for the type and tumor stage of the cells in the sample to be determined. These differentially expressed genes are collectively referred to herein as marker genes. The corresponding gene products are referred to as "marker proteins" or "marker polypeptide". The marker genes for oral cancer include urokinase plasminogen activator, oncofetal trophoblast glycoprotein, cathepsin L, Wilms tumor related protein, FAT, GRO2, AML1, heat shock protein 90, crystallin alpha-B, aldehyde dehydrogenase-9, aldehyde dehydrogenase-10, carboxylesterase-2, cytochrome p450 and others shown in Table 1."

In addition, the specification on page 12, lines 5-9, teaches that "[T]o generate a test expression profile from a biological sample obtained from a patient, the expression levels of a plurality of genes associated with an oral disease need to be determined. In one embodiment, the plurality of genes used is the set of 45 HPE genes that Applicants have demonstrated to be differentially expressed in oral cancer samples versus normal samples (See Table 1 for a list of the 45 genes)." Applicants further point out that Table 1 on pages 79-81 lists the accession numbers for the 45 genes in Table 1.

Applicants believe that the claim amendments have obviated the written description rejection. In view of the teachings of the specification, one of skill in the art would readily

appreciate that Applicants were in possession of the claimed invention at the time this application was filed. Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections for lack of written description.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 5-6, 8-10, and 33-37 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Solely to expedite prosecution, Applicants have amended certain claims. Such amendments are not made in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

A. The Examiner asserts that the recitations of "at least 40 genes" and "at least 5 genes" in claims 1 and 33 are an open-ended ranges that encompasses any group comprising more than 5 or more than 40 genes. In response, Applicants have amended claim 1 and canceled claim 33-37 to remove such recitations, rendering the rejection moot.

B. The Examiner asserts that it is not clear whether any of SEQ ID NOs: 1-43 is "the full-length sequence required or only part of the sequence." In response, Applicants have amended claim 1 and canceled claim 33-37 to remove the recitations of SEQ ID NOs, rendering the rejection moot.

C. The Examiner asserts that it is not clear whether claim 8 requires all 43 sequences of SEQ ID NOs: 1-43 or includes subsets of these sequence? In response, Applicants have canceled claim 8, rendering the rejection moot. Further, Applicants submit that independent claim 1 as amended is clearly directed to a method which requires all 45 genes.

D. The Examiner asserts that the scope of claim 33 is not clear because the claim is both open (i.e., "at least 5 genes") and closed (i.e., "consist"). In response, Applicants have canceled claim 33, rendering the rejection moot.

E. The Examiner asserts that the scope of claim 1 is not clear because the claim is both open (i.e., "at least 40 genes") and closed (i.e., "consist"). First of all, Applicants point out that claim 1 does not recite the term "consist." Nonetheless, as described above, Applicants have amended claim 1 to remove the recitation of "at least 40 genes", rendering the rejection moot.

F. The Examiner asserts that it is not clear whether claim 36 requires all 14 sequences or includes subsets of these sequences. As described above, Applicants have canceled claim 36, rendering the rejection moot.

In view of the above amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw all rejections under 35 U.S.C. § 112, second paragraph.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-6, 8, 10, and 33-37 are rejected for alleged lack of enablement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Examiner asserts that "[t]he working examples on pages 69-80 state that the '45 genes are strongly correlated with the appearance of malignancy in oral epithelium' (page 69, lines 9-10) and 'the 45 genes . . . exhibit close association with oral cancer development (page 72, lines 27-28). It is noted: that only 43 sequences or less are present in the claims . . . In addition, a specific subset of genes or a minimum number of specific genes that are diagnostic are not provided in the original specification." See Office Action, page 15, lines 18-19; and page 16, lines 1-10.

As described above, independent claim 1 as amended recites a method using all 45 genes which are clearly identified by their accession numbers provided in Table 1 (pages 79-81). Claims 8 and 33-37 have been canceled without prejudice. Applicants believe that the claim amendments have obviated this enablement rejection.

The Examiner further asserts that "[w]hile techniques for expression profiling (i.e., screening for gene expression) are well known in the art, specific genetic markers to diagnose oral cancer are

not well known in the art. Thus, applicants are enabled for screening for gene expression, but have not provided an enabling disclosure for diagnosing oral cancer." See Office Action, page 16, lines 10-13.

Applicants respectfully disagree. The specification is enabling for the full scope of the method as recited in amended claim 1. The specification provides working examples to show that all the 45 genes in Table 1 were differently expressed in oral cancer patients (e.g., pages 69-80). As such, one of skill in the art would know that the expression profile of these 45 genes (e.g., claim 1) could be successfully used for diagnosis of an oral cancer. Moreover, the specification teaches how to measure the gene expression levels in a biological sample and how to compare the test expression profile with a signature expression profile of these 45 genes from a patient known to have an oral cancer. Further, the level of skill in the art was high at the time of the filing date of the present application. The techniques involved in the invention, all of which were well known in the art even before the filing date, are highly reliable and can be readily practiced by a skilled artisan.

Further, Applicants point out that, "[I]n order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." (MPEP 2164.04).

In this case, the Examiner has not provided adequate reasoning to support the contention that the claims are not enabled for a method for diagnosing an oral cancer as recited in amended claim 1. As described above, the specification provides working examples demonstrating that the expression profile of these 45 genes could be successfully used for diagnosis of an oral cancer in a patient.

Applicants note that the Examiner has cited several references to raise the enablement rejection. However, these cited references are irrelevant and do not support the enablement rejection. None of the cited references relate to a method which uses all the 45 genes as recited in claim 1 for diagnosing an oral cancer. The Examiner has not provided any reasoned basis on which to doubt that the instantly claimed methods would be operative, thereby failing to meet the burden of establishing a *prima facie* case of lack of enablement.

In sum, Applicants' specification teaches how to carry out the claimed methods, and there is no undue experimentation necessary to practice the full scope of the method as recited in amended independent claim 1. In the absence of probative evidence to the contrary from the Examiner, the data in the instant specification favors a finding of the enablement of the claimed method. Applicants submit that the pending claims as amended are enabled throughout their scope. Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection.

CONCLUSION

In view of the above remarks, Applicants believe that the pending application is in condition for allowance. Applicants believe that no fee is due. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. **MIN-P01-042** from which the undersigned is authorized to draw.

Dated: 2/13/09

Respectfully submitted,

By _____

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